## SEQ. ID. NO.:1

AAGCTTAATTGGGGGCCAAGTAGACAGCAGGACATTCAGTGTGCCTTGTTTCCTTTGTCTTTTGGCTCCA GGTATCAGCAAGCCAAACAAAGGCCCCTCATCTAAGCTGTGTTCTTCAGGCCCTACCTCCAGCGCCCAGAA TGAGCCTATTGGCCCCCACAGCTCTCAGGAGCAAGAGTGATGTACAGGACATTGTGAGCAAGAAGTGGGT GCTGCAAACTGCATAACCCCCCTCCTACCGGCAAGACACCGAGTGCTCACACAGAGCTTACTCGTAGGAC TTGCCAGCTGGTTAAGACACCCCTGCCATTTTCTCTAACAAGCAGGAGTTCAGTTCAGTTCACAGGGAT TCCCCCTATTTAAGTCCAGCGCTCTGTGCTTTAGTTGATCCCTGGTGTCTCGTGTCTTTGTCTGCTGCTG CCGAGGCCCTGGATGCTGCCAAGAAGCTGCAGCCCATTCAGACATCAGCTAAGAACCTCATCATCTTCCT GGGTGACGGTGAGTGTGTGAGCGAGGCCTGCCACCCTGGGGCCCTTGTACTCCAAGTACCCAGGGCCACT GGTGGGTACGGACAGGCCTCAGGGTTCAGTCCTGACGAGGTTCTGCTCCTTCAGGAATGGGGGTACCAAC AGTGACAGCCACCAGGATCCTAAAGGGACAGTTGGAAGGTCATCTAGGACCTGAGACACCCCTAGCCATG GACCGCTTCCCATATATGGCTCTGTCCAAGGTGAGTTCTTAGCCACATCTGAAATGACTGATGGGATCCA TCCCCAGACATACAGTGTGGACAGACAGGTTCCAGACAGTGCAAGCACGGCCACCGCCTACCTGTGTGGG GTCAAGACCAACTACAAGACCATCGGCTTGAGTGCAGCCGCGAGATTCGACCAGTGCAACACCACATTTG GCAATGAGGTCTTCTCAGTGATGTACCGTGCCAAGAAAGCAGGTGAGTTGGAGCCAGGCTCAGCTATGGG GGGCAAGCCTAGGGGACTGGATGTCTCACCCTGACCTTTGCCGTCTTCAGGAAAATCCGTAGGTGTGGTG ACCACCACCAGAGTGCAGCACGCCTCTCCCTCGGGCACATATGTTCACACAGTGAACCGCAATTGGTATG GGGATGCTGACATGCCTGCCTCTGCGCTGCGGGAAGGTTGCAAGGACATTGCTACACAACTCATCTCCAA GGGAGGGAGGGGGGGCTCAGGGGGGGGGAAGGGGTGGTCCCAGGCAAACCTTGTAGACTGAAC TCCCTGGATCTTCTGGGGTCTTTGAGGGCCGGGTAGTTCAGTTCCCACATACCTGGTGAGGAGCTAGGGA CTTGGTGGGGGGCGAAAATACATGTTTCCTGCTGGAACCCCAGACCCCGAGTATCCAAATGATGCTAATG AGACTGGAACCAGATTGGATGGCAGGAATCTGGTGCAGGAATGGCTGTCAAAGCACCAGGTGACCGACTG CAGAATATTAGTGATACAGTGGAGACCAGGGAAGGGCTTTGAACCTTACCAGTTGCTTATGTCCCTCTAG GGATCCCAGTATGTTTGGAATCGTGAACAACTCATTCAGAAGGCCCAGGATCCGTCAGTGACATACCTCA TGGGTAATGGCCCCACACTTCCTGCACTGGTACACCTCACATGGCAACCACTGATCCTCTGTGTATATAT GTACCGTGACCCCACTGCCAAGCTTGGTGGTCACCAGTATATATTTTGGTTTTGTACCTCAGGCCTCTTT GAGCCTGTAGACACAAAATTTGATATTCAACGAGATCCCCTGATGGACCCATCTCTGAAGGATATGACAG GAGAGGGCCAGCCAGCTCACTAGTGAACGCGACACTCTGACCATAGTCACTGCTGACCACTCCCATGTCT TCTCCTTTGGTGGCTACACACTTCGAGGGACCTCCATCTTCGGTAGGTTCGGGAACAGTGGCAGGCTGTC TGTGGGGATCTAGCAACGACTGAACCACTGGCCAGGCAAAAGGCGGGGGCTCGTCTAAGCATCATTCTTG ACCTCCATCCTGTATGGCAACGGCCCAGGCTATGTCGGTACAGGGGAAAGACCCAACGTCACCGCCGCTG AAAGCAGTGAGTGCGGTGGGTTGCCTGAAGGTCGGGTAGAGGTGACTCAGATCAGAGTCCTCTCC  $\tt CCCACGGCGGGGAGACGTGGCGATATTCGCGCGTGGCCCGCAGGCGCACTTGGTGCACGGGGTGCAGGA$ GCAGAACTACATCGCGCACGTCATGGCCTCTGCAGGCTGCCTGGAGCCCTACACCGACTGCGGCTTGGCA CCCCCTGCAGATGAAAGCCAGACCACCACGACAACCCGCCAGACCACCATCACCACCACCACCACCACCA CCACCACCACACCACCCCGGTCCATAACAGCGCCAGAAGCCTGGGCCCAGCCACCGCCCCGCTGGCTCT GGCGCTGCTGGCCGGAATGCTGATGCTACTACTAGGGGCTCCTGCGGAGTCCTAAACTCCAGCACATCTA GGCTCCACCCACTAGGTCCCACGCCCTCACCTGGTCCTTCCCTTGACCTCAGTGCTCCCTGCATTC

TCCCTGCGGGCTCTACCCCAGGATCCTCTCTCTGTCTTTCTGCTACTGGCCTCATGTCTAGCCCTACCTT GCATTGCAGCTTCCAGGTTCCTCCTACCCAGGCACTCACAAAGGCCAATCACCTCTGAGCTAGCAGCCAG CCTCAGACCCCACAGAGTTACTTCTCCCCAGGCAGCATGACCACCAAGGCCTTGGACCTCCCGGGGCAAT CCGGACTCTCCTTTTGCCCTCATCCATCAGCCCCTAGAAAAAGATAGGATCCCGCAATAATTTGTGGAGG ACCAAACATGCACCTGCCCATTGGCACTTCCTCCGAGCTTGAATCCATCTTACAGGCTCTGTACCCAGGA CTAAGGCACAAGAGAACACAGAGAGAGGCTGTCTTCCCACTACTCCTCGGTCTAATCTGCTGGCAGGTGG CACATTCAAAACCATCATGGCTCAGCCATACCAACCCACAGAGCGAAGATTCTGAAATCGTTCAGCCCTT TCATGTCTATTGCCCAGCTAGGAGATTCAAAGAGCTGTACCCCACCCCACTCTCAGGTCATCTCAGGTTG CACCTAAATTTCTGAACTGAGAAAAGTCCCTAACTTCCCAGGTCTGCATTCCCCTGGGGAGAGTCAAGTC TAGTGCCTGCTAGGAACGTGCTCTGCCACTGATCCATAGCCCCATATCATCTCCTCCCCTCCCCTCTCCT  $\tt CCTCCCTCTTCCCCTCCTCCTCCTATGACTCTGTAGCCCAAGCTGGCCTCAAATTTATGACAGT$  $\tt CCACTTGCTACAGTCTCCCAGATGCTGGATTTTAAGTGTGAGCCACACTCCTAGCATCTTAGTAGGACCT$  $\verb|TTGCAGAAGGAAAGCCTGAAGTGTCTGGAGCACTGAGTTCAGATGGGGGGAGGGGTAATAGTGGAGCCTCA|$ GTTGGAGAGACAGCCAGCTGAGCAAGATCCTGAATGAGGTGAAGGCCTGAGCCAACACCACACAGCAG  $\tt TGCTAATCCCCCACCCCCAGGCCAGCGATCAGCTGGAAGGTTGCAACGACTGGGTCAGAGAGGGTGGCT$ GGGACAGAGGATGCAAAGCTGGAGCTGCAAGGAGCTGTGGGAGGAGGAAGAACTTTAAAATCCATGGC AGTGTGGTCACAAGCCTTTGAATAAGAATTCAGGACGTGGTACTTTTTCTATTGCAGGAAATATGCAATC GCCAGAGGGGAGATGCAGACCCTAACCATCTCTGACTTGCATTGGAACTTGGTGGAGCACCACCCCAGTA TAGTTCTTGGCCCCTGTCTAACCTGCCCAATGAGGACATTTGAAGGAATTACGTAAAGGTGGATTAAGCT GTGTTTCTCAGTAAGTTTTGCAACACTACAAATTTATCTGTACATTTATGAAGGTACAAAAACACACTTT GCTCCCACTAGTAATATTAGGAAGATTGAATATGCATCCTTATTTGCTAAAATCTTGATTTAACACTGTG AAACATCAATTCGAAATCTTGGCTCTCGGAGTAGTTTATTTCAATTCCGGATTTTAGTGGCTGTCGAGAA AATATGGGAGCTGAATGGAAAAAGGCCATCGTTAACAAAGCTT

## SEQ. ID. NO.:2

MQGPWVLLLLGLRLQLSLSVIPVEEENPAFWNKKAAEALDAAKKLQPIQTSAKNLIIFLGDGMGVPTVTAT RILKGQLEGHLGPETPLAMDRFPYMALSKTYSVDRQVPDSASTATAYLCGVKTNYKTIGLSAAARFDQCNT TFGNEVFSVMYRAKKAGKSVGVVTTTRVQHASPSGTYVHTVNRNWYGDADMPASALREGCKDIATQLISNM DINVILGGGRKYMFPAGTPDPEYPNDANETGTRLDGRNLVQEWLSKHQGSQYVWNREQLIQKAQDPSVTYL MGLFEPVDTKFDIQRDPLMDPSLKDMTETAVKVLSRNPKGFYLFVEGGRIDRGHHLGTAYLALTEAVMFDL AIERASQLTSERDTLTIVTADHSHVFSFGGYTLRGTSIFGLAPLNALDGKPYTSILYGNGPGYVGTGERPN VTAAESSGSSYRRQAAVPVKSETHGGEDVAIFARGPQAHLVHGVQEQNYIAHVMASAGCLEPYTDCGLAPP ADESQTTTTTRQTTITTTTTTTTTTTTTTTPVHNSARSLGPATAPLALALLAGMLMLLLGAPAES

## FIGURE 1B

Underlined = deleted in targeting construct

**Bold** = sequence flanking Neo insert in targeting construct

AAGCTTAATTGGGGGCCAAGTAGACAGCAGGACATTCAGTGTGCCTTGTTTCCTTTGTCT TTTGGCTCCAGGTATCAGCAAGCCAAACAAAGGCCCCTCATCTAAGCTGTGTTCTTCAGG CCTACCTCCAGCGCCCAGAATGAGCCTATTGGCCCCCACAGCTCTCAGGAGCAAGAGTGA TGTACAGGACATTGTGAGCAAGAAGTGGGTGCTGCAAACTGCATAACCCCCCCTCCTACCG GCAAGACACCGAGTGCTCACACAGAGCTTACTCGTAGGACTTGCCAGCTGGTTAAGACAC CAGGATGGCCACTTTGATCACATGGGAGGGGGGGTGTTGTGCAGTTAGGAACAAAGTC TCCCCCTATTTAAGTCCAGCGCTCTGTGCTTTAGTTGATCCCTGGTGTCTCGTGTCTTTG TCTGCTGCTGTCCCGCCACCAGCCCAGCCATGCAGGGACCCTGGGTGCTGCTGCTG GGCCTCAGGCTACAGCTGTCCCTTAGTGTCATTCCAGGTAATGAGGCTCCTTCCAATGAA CACCCATTCCCACCCATGGACCCTTCATGCTGACCCTTCCTCTGCTATTCCCTTGGCCA GTGGAGGAGGAGAACCCGGCCTTCTGGAACAAGAAGGCAGCCGAGGCCCTGGATGCTGCC AAGAAGCTGCAGCCCATTCAGACATCAGCTAAGAACCTCATCATCTTCCTGGGTGACGGT GAGTGTGTGAGCGAGGCCTGCCACCCTGGGGCCCTTGTACTCCAAGTACCCAGGGCCACT GGTGGGTACGGACAGGCCTCAGGGTTCAGTCCTGACGAGGTTCTGCTCCTTCAGGAATGG GGGTACCAACAGTGACAGCCACCAGGATCCTAAAGGGACAGTTGGAAGGTCATCTAGGAC CTGAGACACCCCTAGCCATGGACCGCTTCCCATATATGGCTCTGTCCAAGGTGAGTTCTT  ${\tt AGCCACATCTGAAATGACTGATGGGATCCAGGGCAAGGGAGGCAGAGGGCTCGGGTGAAA}$ GAAATAAATGTCTGCTTTGAGCCCAGTTGGGGTGTCTCTGTCCCCAGACATACAGTGTGG  ${\tt ACAGACAGGTTCCAGACAGTGCAAGCACGGCCACCGCCTACCTGTGTGGGGTCAAGACCA}$ ACTACAAGACCATCGGCTTGAGTGCAGCCGCGAGATTCGACCAGTGCAACACCACATTTG GCAATGAGGTCTTCTCAGTGATGTACCGTGCCAAGAAAGCAGGTGAGTTGGAGCCAGGCT CAGCTATGGGGGGCAAGCCTAGGGGACTGGATGTCTCACCCTGACCTTTGCCGTCTTCAG GAAAATCCGTAGGTGTGGTGACCACCACCAGAGTGCAGCACGCCTCTCCCTCGGGCACAT GGGAAGGTTGCAAGGACATTGCTACACAACTCATCTCCAACATGGACATTAATGTAAGGA GGGAGGTCAGGGGGGTCAAGGGGGGAAGGGGTGGTCCCAGGCAAACCTTGTAGACTGAAC TCCCTGGATCTTCTGGGGTCTTTGAGGGCCGGGTAGTTCAGTTCCCACATACCTGGTGAG CTCTCTGACCACAGGTGATCCTTGGTGGGGGGGGGAAAATACATGTTTCCTGCTGGAACCC CAGACCCCGAGTATCCAAATGATGCTAATGAGACTGGAACCAGATTGGATGGCAGGAATC TGGTGCAGGAATGGCTGTCAAAGCACCAGGTGACCGACTGCAGAATATTAGTGATACAGT GGAGACCAGGGAAGGGCTTTGAACCTTACCAGTTGCTTATGTCCCTCTAGGGATCCCAGT ATGTTTGGAATCGTGAACAACTCATTCAGAAGGCCCAGGATCCGTCAGTGACATACCTCA TGGGTAATGGCCCCACACTTCCTGCACTGGTACACCTCACATGGCAACCACTGATCCTCT GTGTATATATGTACCGTGACCCCACTGCCAAGCTTGGTGGTCACCAGTATATATTTTGGT TTTGTACCTCAGGCCTCTTTGAGCCTGTAGACACAAAATTTGATATTCAACGAGATCCCC TGATGGACCCATCTCTGAAGGATATGACAGAGACGGCCGTGAAAGTGCTAAGCAGGAACC CCAAAGGCTTTTATCTCTTTGTGGAGGGTGAGTCTCCAAGCTCCCATGGAAAGAGGGGAC AATGGACAGGGACAGGCTCAAGCTCACTGGCTTCCTGCAGGGGGCCGAATCGACCGTGGT CACCATCTGGGCACAGCTTATCTGGCGCTGACTGAGGCTGTGATGTTCGACTTAGCCATC GAGAGGGCCAGCCACTACTAGTGAACGCGACACTCTGACCATAGTCACTGCTGACCAC TCCCATGTCTTCTCCTTTGGTGGCTACACACTTCGAGGGACCTCCATCTTCGGTAGGTTC GGGAACAGTGGCAGGCTGTCAATTACGTACAGAATACTTCTGAGCCATCGTTTTCTCTGT CTGTAAAATGGACAGAAATGGCACCTGCCTTGTGGGGATCTAGCAACGACTGAACCACTG GCCAGGCAAAAGGCGGGGGCTCGTCTAAGCATCATTCTTGGCAGGAAAAAGTGTCCCTCT TCCCCCATGCAGGGCTGGCTCCCCTCAATGCTCTGGACGGCAAGCCCTACACCTCCATCC TGTATGGCAACGGCCCAGGCTATGTCGGTACAGGGGAAAGACCCAACGTCACCGCCGCTG AAAGCAGTGAGTGCGGTGGGGTGGCTTGCCTGAAGGTCGGGTAGAGGTGACTCAGATCAG TGTGCCGGTGAAGTCGGAGACCCACGGCGGGGAGGACGTGGCGATATTCGCGCGTGGCCC GCAGGCGCACTTGGTGCACGGGGTGCAGGAGCAGAACTACATCGCGCACGTCATGGCCTC TGCAGGCTGCCTGGAGCCCTACACCGACTGCGGCTTGGCACCCCCTGCAGATGAAAGCCA AACCACCCGGTCCATAACAGCGCCAGAAGCCTGGGCCCAGCCACCGCCCCGCTGGCTCT GGCGCTGCTGGCCGGAATGCTGATGCTACTACTAGGGGCTCCTGCGGAGTCCTAAACTCC AGCACATCTAGGCTCCACCCACTAGGTCCCACGCCCTCACCTGGTCCTTCCCTTGA TGCTACTGGCCTCATGTCTAGCCCTACCTTGCATTGCAGCTTCCAGGTTCCTACCCA CTTCTCCCCAGGCAGCATGACCACCAAGGCCTTGGACCTCCCGGGGCAATCCGGACTCTC CTTTTGCCCTCATCCATCAGCCCCTAGAAAAAGATAGGATCCCGCAATAATTTGTGGAGG ACCAAACATGCACCTGCCCATTGGCACTTCCTCCGAGCTTGAATCCATCTTACAGGCTCT GTACCCAGGACTAAGGCACAAGAGAACACAGAGAGAGGGCTGTCTTCCCACTACTCCTCGG AGTTCTTCCTCGATGTCTCTGGACCAGCTCCACATTCAAAACCATCATGGCTCAGCCATA CCAACCCACAGAGCGAAGATTCTGAAATCGTTCAGCCCTTTCATGTCTATTGCCCAGCTA GGAGATTCAAAGAGCTGTACCCCACCCCACTCTCAGGTCATCTCAGGTTGCACCTAAATT TCTGAACTGAGAAAAGTCCCTAACTTCCCAGGTCTGCATTCCCCTGGGGAGAGTCAAGTC AATAATAAAAGAATGTATTCAATACAATAGCAATAGTCATTTTCTTTTCTTCGGCTCAA AACCAGAGCCTAGTGCCTGCTAGGAACGTGCTCTGCCACTGATCCATAGCCCCATATCAT AGCCCAAGCTGGCCTCAAATTTATGACAGTCCACTTGCTACAGTCTCCCAGATGCTGGAT TTTAAGTGTGAGCCACACTCCTAGCATCTTAGTAGGACCTTTGCAGAAGGAAAGCCTGAA GTGTCTGGAGCACTGAGTTCAGATGGGGGGGGGGTAATAGTGGAGCCTCAGTTGGAGAGA GACAGCCAGCTGAGCAAGATCCTGAATGAGGTGAAGGCCTGAGCCAACACCACACAGCAG TGCTAATCCCCCACCCCCAGGCCAGCGATCAGCTGGAAGGTTGCAACGACTGGGTCAGA GAGGGTGGCTGGGACAGAGGATGCAAAGCTGGAGCTGCAAGGAGCTGTGGGAGGAGAGA AGAACTTTAAAATCCATGGCAGTGTGGTCACAAGCCTTTGAATAAGAATTCAGGACGTGG ATGGGGGGTGGGAATGGGTGTTAGATATAGGAGCTGGTCAGCCAGAGGGGAGATGCAGAC  $\verb|CCTAACCATCTCTGACTTGCATTGGAACTTGGTGGAGCACCACCCCAGTATAGTTCTTGG|$ CCCCTGTCTAACCTGCCCAATGAGGACATTTGAAGGAATTACGTAAAGGTGGATTAAGCT GTGTTTCTCAGTAAGTTTTGCAACACTACAAATTTATCTGTACATTTATGAAGGTACAAA AACACACTTTGCTCCCACTAGTAATATTAGGAAGATTGAATATGCATCCTTATTTGCTAA AATCTTGATTTAACACTGTGAAACATCAATTCGAAATCTTGGCTCTCGGAGTAGTTTATT TCAATTCCGGATTTTAGTGGCTGTCGAGAAAATATGGGAGCTGAATGGAAAAAGGCCATC GTTAACAAAGCTT

FIGURE 2B

## 

Gene Sequence Structure \*

Size of genomic: 5293 bp

570 bp Sequence Deleted 669 bp

Targeting Vector\* (genomic sequence)
Construct Number: 2109

Arm Length: 5': 1.1 kb 3': 3.3 kb

Good is

3. am

Cassette

S and

LacZ-Neo

> Targeting Vector Endogenous Locus

\* Not drawn to scale

5 ·> GAGAACCCGGCCTTCTGGAAC
AAGAAGGCAGCCGAGGCCCTGGAT
GCTGCCAAGAAGCTGCAGCCCATT
CAGACATCAGCTAAGAACCTCATC
ATCTTCTGGGCGACGTGAGTGT
GTGAGCGAGGCCTGGCCACCTGG
GGCCCTTGTACTCCAGGCCACCCTGG
GGCCCTTGTACTCCAGGCCACCCTGG
GGCCATGTACTCCAAGTACCCAG
GGCCACTGTACTACAGATACCCAG
CTCAGGGTTCAA3 ·

FIGURE 2C